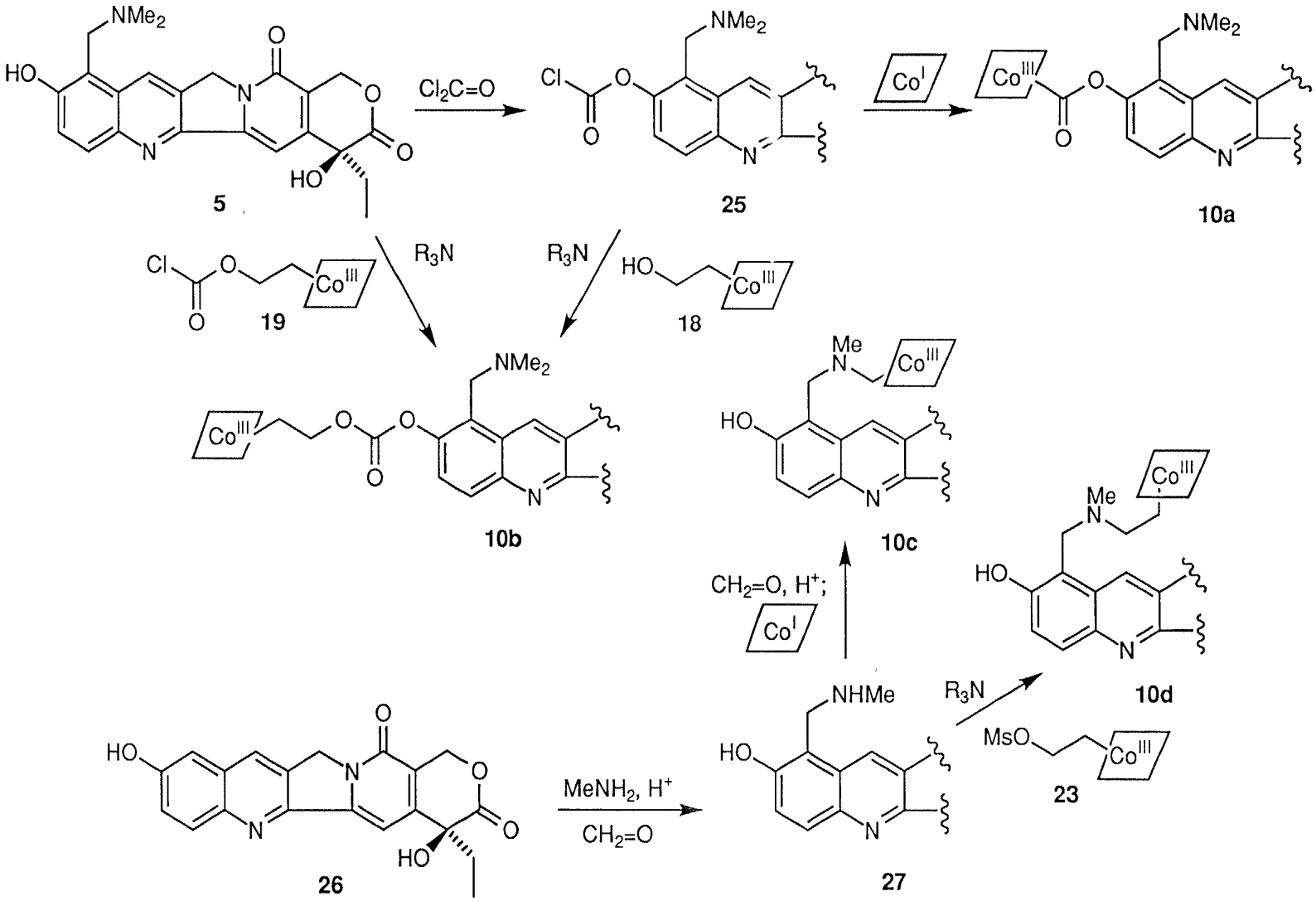
product camptothecin to **5** can be modified at the appropriate point to allow for attachment of the cobalt complex. The first three steps to prepare phenolic intermediate **26** are known (Mulliez et al., 1994). Mannich-type substitution with formaldehyde/dimethylamine then gives **5**. Use of methylamine gives the corresponding secondary amine **27**. At this point, linkage to Co via a methylene to give **10c** is possible via Co(I) trapping of a second, *in situ* generated imminum salt. Alternatively, N-alkylation with **23** gives **10d**. Cleavage of **10a** and **10b** provides **5** directly via fragmentative pathway or indirectly via other products. Cleavage of **10c** with hydrogen extraction yields **5**. Cleavage of **10d** yields the product **5** having an ethylmethylamino group in place of the dimethylamino group.


NMe2
HO
O
N
O
O
HO
5
Cl2C=O
Cl
O
O
N
25
Co^I
Co^III
10a
Cl
O
O
Co^III
19
R3N
R3N
HO
Co^III
18
Co^III
O
O
10b
Me
N
Co^III
HO
10c
CH2=O, H+;
Co^I
Co^III
Me
N
HO
10d
R3N
MsO
Co^III
23
HO
O
N
O
O
HO
26
MeNH2, H+
CH2=O
NHMe
HO
27

A busulfan-containing bioconjugate car be synthesized by the following method. Busulfan is an alkylating agent used therapeutically against chronic myelogenous leukemia (CML). The preferred point for attaching busulfan to the organocobalt complex is on one of the alkanesulfonate units. A slight change in the structure of the sulfonate portion of the ester is will not exert a large effect on the ability of the released drug to crosslink DNA. Cleavage of **7a** followed by hydrogen abstraction furnishes the mixed ethanesulfonate/methanesulfonate **2b**. Trapping of the carbon radical under oxidative conditions produces mixed bis(sulfonate) **2c**, which is also a competent crosslinking agent. Cleavage of **7b** results in the release of the parent drug **2a** after hydrogen abstraction.

Bis-methylsulfonate busulfan is conjugated to cobalamin, Co[SALEN] and other organocobalt complexes according to the following reaction schemes. For the preparation of **7a**, the commercially available sodium salt of bromoethanesulfonic acid (**11**) serves as the starting point. Heating with phosphorus pentachloride furnishes the corresponding sulfonyl chloride **12** as a distillable liquid. Treatment with Co(I) leads to preferential displacement of the bromide to furnish **13**, which is converted to **7a** by sequential treatment with 1,4-butanediol and mesyl chloride. The order of the final three steps can be changed; for example, treatment of **12** with excess butanediol, followed by mesyl chloride gives the mixed bis(sulfonate) **14**. Selective displacement of the primary bromide by Co(I) then gives **7a**. In the case of conjugate **7b**, treatment of 2-bromobutane-1,4-diol (which is readily available from malic acid diester) with Co(I) gives adduct **15**. Bis(mesylation) gives **7b**. Alternatively, **7b** is prepared from **16** (X = Br or I) with selective displacement of the halide.